**Table S1** The clinic-characteristics of 102 patients with CRC

|  |  |  |
| --- | --- | --- |
| **Clinic pathological characteristics** | **Number of Cases/Value** | **%** |
| Primary tumor site |  |  |
| Colon | 62 | 60.78 |
| Rectum | 40 | 39.22 |
| Colon location |  |  |
| Right | 30 | 29.41 |
| Left | 72 | 70.59 |
| Gender |  |  |
| Male | 71 | 69.61 |
| Female | 31 | 30.39 |
| Age |  |  |
| less than 60 | 56 | 54.9 |
| more than 60 | 46 | 45.1 |
| Initial stage |  |  |
| Advanced | 53 | 51.96 |
| Recurrence | 49 | 48.04 |
| Survival statues |  |  |
| Death | 48 | 47.06 |
| Alive | 54 | 52.94 |
| Primary tumor resection |  |  |
| Radical | 53 | 51.96 |
| Palliative | 49 | 48.04 |
| Anti-EGFR therapy |  |  |
| Yes | 52 | 50.98 |
| No | 50 | 49.02 |
| Success staining |  |  |
| IRF-3 | 102 | 100.00 |
| IRF-7 | 97 | 95.01 |
| CD19 | 94 | 92.16 |
| CD4 | 96 | 94.12 |
| CD8 | 98 | 96.08 |
| CD68 | 101 | 99.02 |
| MPO | 92 | 90.20 |
| CD21 | 96 | 94.12 |
| Average H score |  |  |
| IRF-3 | 99.22 | / |
| IRF-7 | 91.36 | / |
| CD19 | 37.95 | / |
| CD4 | 20.30 | / |
| CD8 | 8.98 | / |
| CD68 | 23.54 | / |
| MPO | 34.88 |  |
| CD21 | 11.79 |  |
| Median H score |  |  |
| IRF-3 | 101.97 | / |
| IRF-7 | 93.86 | / |
| CD19 | 29.93 | / |
| CD4 | 14.43 | / |
| CD8 | 3.98 | / |
| CD68 | 16.41 | / |
| MPO | 29.91 |  |
| CD21 | 11.12 |  |
| Total | 102 | 100 |

**Table S2** One hundred and twenty-six differentially expressed genes (DEGs) between low- and high-risk scores according to IRF family

|  |  |  |  |
| --- | --- | --- | --- |
| **Gene** | **Log2 [Fold Change]** | ***P* value** | **Regulated** |
| PSCA | 2.084 | 2.174E-25 | UP |
| CD177 | -1.867 | 4.294E-23 | DOWN |
| TRPV6 | 2.020 | 3.359E-20 | UP |
| AQP5 | 1.848 | 2.631E-17 | UP |
| JCHAIN | -1.337 | 6.393E-17 | DOWN |
| C8G | 1.027 | 3.187E-16 | UP |
| MUC6 | 1.807 | 6.451E-16 | UP |
| M1AP | 1.251 | 2.985E-15 | UP |
| ZG16 | -1.742 | 6.880E-15 | DOWN |
| PPBP | -1.752 | 8.478E-15 | DOWN |
| SLC22A31 | 1.378 | 2.144E-14 | UP |
| GJA3 | 1.119 | 2.686E-13 | UP |
| DNASE1L3 | -1.080 | 4.428E-13 | DOWN |
| TM4SF4 | 1.262 | 4.722E-13 | UP |
| ONECUT3 | 1.926 | 8.546E-13 | UP |
| AC136428.1 | -1.238 | 2.803E-12 | DOWN |
| GPR15 | -1.202 | 4.385E-12 | DOWN |
| KRT16 | 1.229 | 3.753E-11 | UP |
| CA4 | -1.360 | 5.290E-11 | DOWN |
| PRSS56 | -1.892 | 1.011E-10 | DOWN |
| MSLNL | 1.331 | 2.202E-10 | UP |
| ARHGAP40 | 1.333 | 2.690E-10 | UP |
| LINC01314 | 1.203 | 2.775E-10 | UP |
| MYRFL | 1.080 | 4.069E-10 | UP |
| CEBPE | -1.041 | 4.871E-10 | DOWN |
| SCNN1B | -1.012 | 5.910E-10 | DOWN |
| PYY | -1.331 | 1.360E-09 | DOWN |
| GALNT9 | 1.093 | 1.532E-09 | UP |
| RPE65 | 1.337 | 1.757E-09 | UP |
| TMPRSS11E | 1.587 | 2.253E-09 | UP |
| ADGRD2 | 1.021 | 3.211E-09 | UP |
| AC007040.2 | 1.122 | 4.172E-09 | UP |
| OTOP2 | -1.502 | 5.179E-09 | DOWN |
| HBG2 | -1.337 | 6.349E-09 | DOWN |
| KCNC2 | 1.814 | 8.729E-09 | UP |
| KCNQ2 | 1.175 | 2.031E-08 | UP |
| GUCA2B | -1.233 | 2.268E-08 | DOWN |
| GJB6 | 1.067 | 2.332E-08 | UP |
| FOXL2 | 1.391 | 2.863E-08 | UP |
| HOXC10 | 1.210 | 2.953E-08 | UP |
| PGPEP1L | 1.481 | 8.146E-08 | UP |
| CDR1 | 1.794 | 1.503E-07 | UP |
| MUC16 | 1.116 | 1.836E-07 | UP |
| CLDN8 | -1.569 | 3.159E-07 | DOWN |
| NMUR2 | 1.296 | 4.015E-07 | UP |
| IL22 | -1.133 | 4.195E-07 | DOWN |
| CYP7A1 | 1.412 | 5.247E-07 | UP |
| CALB1 | 1.142 | 5.291E-07 | UP |
| DPCR1 | 1.105 | 6.723E-07 | UP |
| LHX1 | 1.513 | 7.035E-07 | UP |
| CA1 | -1.127 | 1.005E-06 | DOWN |
| ANXA10 | 1.223 | 1.182E-06 | UP |
| IFNL1 | 1.066 | 1.216E-06 | UP |
| MS4A12 | -1.058 | 1.476E-06 | DOWN |
| INSL5 | -1.496 | 2.128E-06 | DOWN |
| KRT14 | 1.204 | 2.233E-06 | UP |
| ACTBL2 | 1.033 | 3.161E-06 | UP |
| INSL4 | -1.739 | 3.235E-06 | DOWN |
| APOA4 | 1.747 | 3.567E-06 | UP |
| C12orf40 | 1.580 | 4.518E-06 | UP |
| SEMG1 | 1.116 | 4.822E-06 | UP |
| SLC36A2 | 1.317 | 6.693E-06 | UP |
| SFTPC | -1.677 | 7.155E-06 | DOWN |
| CYP1A1 | -1.264 | 7.159E-06 | DOWN |
| ITLN2 | -1.063 | 8.114E-06 | DOWN |
| MSMB | -1.460 | 8.154E-06 | DOWN |
| MAGEA12 | 1.861 | 8.481E-06 | UP |
| C17orf78 | -1.011 | 8.511E-06 | DOWN |
| FGL1 | -1.275 | 1.120E-05 | DOWN |
| SLC38A8 | 1.078 | 1.220E-05 | UP |
| CCK | 1.194 | 1.392E-05 | UP |
| IFNE | 1.117 | 1.421E-05 | UP |
| MAGEB2 | -2.140 | 1.486E-05 | DOWN |
| SPRR1B | 1.168 | 1.730E-05 | UP |
| CPA1 | 1.309 | 1.774E-05 | UP |
| RGR | 1.077 | 1.830E-05 | UP |
| HIST1H4L | 1.551 | 2.427E-05 | UP |
| TMIGD1 | -1.006 | 2.563E-05 | DOWN |
| SMIM18 | 1.021 | 3.250E-05 | UP |
| KRTAP13.2 | -1.422 | 4.308E-05 | DOWN |
| TMPRSS11D | 1.349 | 5.790E-05 | UP |
| DRGX | 1.041 | 5.870E-05 | UP |
| TSPYL6 | 1.500 | 9.071E-05 | UP |
| LBX1 | 1.687 | 1.297E-04 | UP |
| DLK1 | -1.453 | 1.309E-04 | DOWN |
| LIN28A | -1.185 | 1.735E-04 | DOWN |
| SPRR3 | 1.059 | 1.882E-04 | UP |
| T | 1.152 | 4.422E-04 | UP |
| HOXC13 | 1.182 | 5.110E-04 | UP |
| NKX6.3 | 1.162 | 5.851E-04 | UP |
| CSAG1 | 1.271 | 6.739E-04 | UP |
| DEFB4A | -1.072 | 8.875E-04 | DOWN |
| SERPINB13 | 1.874 | 9.513E-04 | UP |
| CLEC2A | 1.552 | 9.839E-04 | UP |
| SLC10A2 | 1.522 | 1.078E-03 | UP |
| IFNL3 | 1.094 | 1.085E-03 | UP |
| OTOP3 | 1.168 | 1.231E-03 | UP |
| MIA.RAB4B | 1.031 | 1.739E-03 | UP |
| CT83 | -1.765 | 1.846E-03 | DOWN |
| MUC7 | 1.130 | 1.868E-03 | UP |
| SEMG2 | 1.118 | 1.915E-03 | UP |
| MROH2B | 1.090 | 2.890E-03 | UP |
| IVL | 1.062 | 3.666E-03 | UP |
| OR1N2 | 2.196 | 3.944E-03 | UP |
| HTN1 | 1.420 | 4.891E-03 | UP |
| XAGE2 | 1.232 | 5.012E-03 | UP |
| RHAG | -1.257 | 5.263E-03 | DOWN |
| SAGE1 | 1.049 | 5.485E-03 | UP |
| TMPRSS11A | 1.181 | 5.611E-03 | UP |
| DCAF8L2 | 1.020 | 5.741E-03 | UP |
| OR6A2 | 1.093 | 6.276E-03 | UP |
| RIPPLY2 | 1.064 | 7.584E-03 | UP |
| GLYATL3 | 1.070 | 7.832E-03 | UP |
| COX7B2 | 1.422 | 9.235E-03 | UP |
| MAGEA3 | 1.088 | 1.049E-02 | UP |
| CLRN1 | 1.082 | 1.073E-02 | UP |
| MAGEA1 | 1.198 | 1.180E-02 | UP |
| DCAF4L2 | 1.827 | 1.232E-02 | UP |
| LIN28B | 1.302 | 1.411E-02 | UP |
| TBC1D3D | 1.277 | 1.516E-02 | UP |
| UBE2U | 1.082 | 2.216E-02 | UP |
| DPPA2 | 1.322 | 2.502E-02 | UP |
| PAGE1 | 1.013 | 3.278E-02 | UP |
| CFHR4 | 1.052 | 3.835E-02 | UP |
| ZNF479 | 1.879 | 4.230E-02 | UP |
| HBZ | -1.189 | 4.234E-02 | DOWN |

**Table S3** GO analysis of identified 126 DEGs base on IRF family scores

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **ONTOLOGY** | **ID** | **Description** | **Count** | ***P* adjust** | **Gene** |
| BP | GO:0015669 | gas transport | 4 | 0.003 | AQP5/HBG2/RHAG/HBZ |
| BP | GO:0019730 | antimicrobial humoral response | 7 | 0.003 | JCHAIN/PPBP/SEMG1/DEFB4A/MUC7/SEMG2/HTN1 |
| BP | GO:0006959 | humoral immune response | 10 | 0.010 | JCHAIN/C8G/PPBP/SEMG1/IFNE/DEFB4A/MUC7/SEMG2/HTN1/CFHR4 |
| MF | GO:0015077 | monovalent inorganic cation transmembrane transporter activity | 9 | 0.020 | SCNN1B/OTOP2/KCNC2/KCNQ2/SLC36A2/SLC10A2/OTOP3/RHAG/COX7B2 |
| MF | GO:0015267 | channel activity | 10 | 0.020 | TRPV6/AQP5/GJA3/SCNN1B/OTOP2/KCNC2/KCNQ2/NMUR2/OTOP3/RHAG |
| MF | GO:0022803 | passive transmembrane transporter activity | 10 | 0.020 | TRPV6/AQP5/GJA3/SCNN1B/OTOP2/KCNC2/KCNQ2/NMUR2/OTOP3/RHAG |
| CC | GO:0005796 | Golgi lumen | 5 | 0.037 | MUC6/ZG16/MUC16/DEFB4A/MUC7 |

**Table S4** KEGG analysis of 126 DEGs base on IRF family scores

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **ID** | **Description** | **Count** | ***P* value** | **Gene** |
| hsa04970 | Salivary secretion | 4 | 0.001097 | TRPV6/AQP5/MUC7/HTN1 |
| hsa00910 | Nitrogen metabolism | 2 | 0.003105 | CA4/CA1 |
| hsa04630 | JAK-STAT signaling pathway | 4 | 0.008134 | IL22/IFNL1/IFNE/IFNL3 |
| hsa05150 | Staphylococcus aureus infection | 3 | 0.011706 | KRT16/KRT14/DEFB4A |
| hsa04060 | Cytokine-cytokine receptor interaction | 5 | 0.014519 | PPBP/IL22/IFNL1/IFNE/IFNL3 |
| hsa04979 | Cholesterol metabolism | 2 | 0.025234 | CYP7A1/APOA4 |
| hsa00140 | Steroid hormone biosynthesis | 2 | 0.036436 | CYP7A1/CYP1A1 |
| hsa00830 | Retinol metabolism | 2 | 0.043215 | RPE65/CYP1A1 |
| hsa04610 | Complement and coagulation cascades | 2 | 0.066027 | C8G/CFHR4 |

**Table S5** Results of Gene Set Enrichment Analysis (GSEA)

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Name** | **Size** | **Enrichment**  **Score** | **NES** | **FDR** | **Leading edge** |
| KEGG\_CYTOKINE\_CYTOKINE\_RECEPTOR\_INTERACTION | 262 | -0.4667 | -2.07015 | 1.37E-08 | tags=37%, list=13%, signal=32% |
| KEGG\_CHEMOKINE\_SIGNALING\_PATHWAY | 187 | -0.49651 | -2.15541 | 1.37E-08 | tags=32%, list=13%, signal=28% |
| KEGG\_HEMATOPOIETIC\_CELL\_LINEAGE | 81 | -0.63767 | -2.40007 | 3.68E-08 | tags=53%, list=13%, signal=46% |
| KEGG\_RIBOSOME | 87 | 0.659957 | 2.079355 | 2.25E-07 | tags=72%, list=22%, signal=56% |
| KEGG\_CELL\_ADHESION\_MOLECULES\_CAMS | 112 | -0.52961 | -2.11776 | 6.82E-06 | tags=49%, list=15%, signal=42% |
| KEGG\_INTESTINAL\_IMMUNE\_NETWORK\_FOR\_IGA\_PRODUCTION | 34 | -0.69524 | -2.2379 | 0.000125 | tags=47%, list=9%, signal=43% |
| KEGG\_ECM\_RECEPTOR\_INTERACTION | 83 | -0.50457 | -1.92497 | 0.00046 | tags=48%, list=13%, signal=42% |
| KEGG\_ASTHMA | 16 | -0.75445 | -2.06291 | 0.009713 | tags=44%, list=8%, signal=40% |
| KEGG\_NEUROACTIVE\_LIGAND\_RECEPTOR\_INTERACTION | 271 | -0.30755 | -1.37737 | 0.02826 | tags=30%, list=11%, signal=27% |
| KEGG\_NITROGEN\_METABOLISM | 23 | -0.63119 | -1.88066 | 0.036352 | tags=30%, list=4%, signal=29% |
| KEGG\_CARDIAC\_MUSCLE\_CONTRACTION | 73 | 0.525865 | 1.627652 | 0.036844 | tags=37%, list=19%, signal=30% |
| KEGG\_PORPHYRIN\_AND\_CHLOROPHYLL\_METABOLISM | 40 | -0.51365 | -1.75836 | 0.036844 | tags=35%, list=13%, signal=31% |
| KEGG\_PRIMARY\_IMMUNODEFICIENCY | 35 | -0.55336 | -1.81013 | 0.036844 | tags=31%, list=7%, signal=29% |

**Table S6** A comparison of differential risk score group calculated by expression level of IRF family in para normal tissues of patients with CRC from TCGA database.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Patients from COAD/READ** | **All patients**  **(n = 51)** | **Low**  **(n = 25)** | **High**  **(n = 26)** | ***P* value** |
| Gender |  |  |  | 0.210 |
| Female | 28 (54.9%) | 11 (44.0%) | 17 (65.4%) |  |
| Male | 23 (45.1%) | 14 (56.0%) | 9 (34.6%) |  |
| Age |  |  |  | 1.000 |
| ＜60 | 12 (23.5%) | 6 (24.0%) | 6 (23.1%) |  |
| ≥60 | 39 (76.5%) | 19 (76.0%) | 20 (76.9%) |  |